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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,952	10/04/2004	Reddy Bandi Parthasaradhi	H1089/20015	3097

3000 7590 10/17/2008

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	

NOTIFICATION DATE	DELIVERY MODE
10/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

Office Action Summary	Application No.	Applicant(s)	
	10/509,952	PARTHASARADHI ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of the office action dated Jan. 17, 2008 is hereby withdrawn in view of the following new grounds of rejection.

Claims 1-4, are pending.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Vidyadhar et al. US 6,649,765.

See col. 4, example 2, the donepezil hydrochloride was dissolved in residue of free base concentrated from methylene dichloride solvent system adding a methanol and methanolic HCl mixture, then the solvents were removed to obtain a "solid", thus, anticipated the claims. Please note that a solid being silent about its crystallinity is noncrystalline or amorphous.
Applicants argued that the term "concentration" is removal of solvents, therefore, the solvents of the prior art process is methylene dichloride, then, methanol not methylene dichloride with methanol. Applicants argued that the default description of a solid material is not inherently "amorphous".

Two chemical handbook are hereby attached for applicants convenience. The CRC handbook defines amorphous as "having no definite order of crystalline structure". Therefore, if a solid was not defined to have "definitive crystalline order" is amorphous. The Hackh's chemical dictionary is provided to show that the term "concentrate" chemically is the increase of solute content, thus, *not removal of all solvent.*

In addition, the Borchardt et al. reference is hereby provided for applicants' convenience. Borchardt et al. taught that it is well recognized by chemists that the first isolated product before crystallization is ordinarily amorphous which is the Oswald's rule. Further continuation patent

of US 6,649,765, the US 7,186,842, referred to the disclosure of the '765 material (see col. 2, lines 33-35) being made in Vidyadhar laboratory being *amorphous*. Therefore, per ponderous of evidence indicated that the noncrystalline material disclosed by Vidyadhar et al. '765 is amorphous even though the term was not used in that patent.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vijyadhar et al. US 6,649,765 in view of Imai et al. US 5,985,864.

Determination of the scope and content of the prior art (MPEP §2141.01)

Vijyadhar et al.'765 disclosed anticipatory process of the claims which has been delineated supra and incorporated by reference.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The broader scope of claims 1 and 4 encompassing mixture of solvents beyond the residue amount or a different choice of combination; or the method of solvent removal being particularly vacuum drying or spray drying are prima facie obvious variation of the Vijyadhar et al.'765 process. It is conventionally known that donepezil hydrochloride are soluble in a variety of solvents (see Imai et al. '864 entire document), and vacuum or spray drying are conventional laboratory choices of solvent removing procedure.

Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of general laboratory skill and the Imai et al. '864 reference would be in possession of the instant claims because a proven process was disclosed by Vijyadhar '765, the optional choices of solvents wherein donepezil hydrochloride is

soluble have been provided by Imai. Therefore, one having ordinary skill would pick and choose any of the solvent or mixture of solvents wherein donepezil hydrochloride is soluble for the process and employ any one of the solvent removing technique for solvent reduction depending on resource availability. Picking and choosing an effect oriented condition in a chemical process is prima facie obvious in the chemical art, especially, such picking and choosing has been conventionally evidenced to be operable. In re Szumski 133 USPQ 551.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugimoto et al. US 4,895,841 or Vijyadhar et al. US 6,649,765, or Imai et al. US 5,985,864 in view of Lieberman et al. and Brittain.

Determination of the scope and content of the prior art (MPEP §2141.01)

Sugimoto et al. (col. 34 example 4) or Vijyadhar et al.'765 (col. 4, example 2) disclosed process of making donepezil hydrochloride of the claims. Imai et al. '864 disclosed multiple variations of modifying the process of making donepezil hydrochloride to obtain variations of crystalline and pure forms of the compound.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the prior art processes and the instant claimed process is that the products being made are crystalline or solids; using mixtures of more limited solvent combinations; and/or the method of solvent removal being particularly vacuum drying or spray drying. It is conventionally known that donepezil hydrochloride is soluble in a variety of solvents (see Imai et al. '864 entire document). It is a conventional teaching that amorphous is more desirable than crystalline form when formulation into pharmaceutical compositions (see Lieberman p.463 last paragraph) and the conventional process for obtaining amorphous material are spray drying or vacuum drying i.e. lyophilization.

Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of Sugimoto '841 or Vijyadhar '765 and the above references by Imai et al. '864, Lieberman and Brittain would be in possession of the instant claims because a proven process of making donepezil hydrochloride in a purified form was disclosed by Sugimoto '841, Vijyadhar '765 or Imai '864. One having ordinary skill in the art in possession of the purified crystalline or solid material of the compound donepezil hydrochloride would be motivated to prepare an amorphous form of the product because it is conventional state of the art that *"Theoretical considerations predict that amorphous solids* ***will*** *in general, be better absorbed than will crystalline ones"* (see Liberman p.463) and the procedure for obtaining amorphous forms have been conventionally well delineated using a spray drying or vacuum drying process (Brittain).

In view of factual evidence provided supra, one having ordinary skill, being motivated by obtaining a better absorbed amorphous form, would pick and choose any of the conventional combinations of solvents wherein donepezil hydrochloride is soluble, then, employ any one of the solvent removing technique for solvent reduction depending on resource and availability, with the expectation of obtaining an "amorphous" form of the product; the claims would have been obvious because an ordinary skilled person "has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." KSR 82 USPQ2d 1385, 1390.

The above references provided:

--*teaching* from the art that donopezil hydrochloride is soluble in chlorinated solvent and alcohol specifically, methylene chloride and methanol;

--*suggestion* that spray dry a pharmaceutical product using a soluble solvent and spray drying procedure would produce an amorphous material;

--*motivation* that an amorphous material would give better dissolution.

Therefore, every element required by the KSR guideline has been provided. To obviate an established prima facie case of obviousness, applicants must provided factual evidence that why a process employed a simultaneously co-existed mixture of chlorinated solvent and alcohol would produce an amorphous material which is different from the amorphous solid found in the prior art using a stepwise introduced dichloromethane and methanol solvents, when both solvents are known to dissolve donopezil hydrochloride.

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Oct. 2, 2008

/Celia Chang/
Primary Examiner
Art Unit 1625